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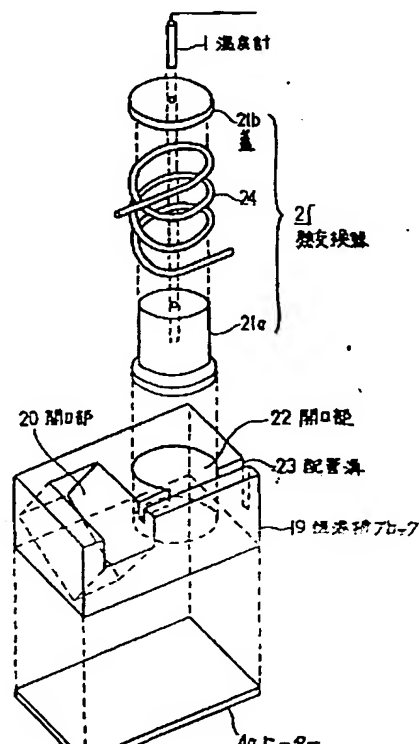
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(54)【発明の名称】 バイオセンサ用恒温槽

(57)【要約】 (修正有)

【目的】 水を熱媒体として一定温度を保つ恒温槽は、マグネティックスターラーや攪拌子などが必要であり、占有体積も大きく保守管理の点でも手間がかかるので、熱媒体に水を用いることなく保守が容易でコンパクトなものにする。

【構成】 本発明のバイオセンサ用恒温槽は、金属製の恒温槽ブロック19の一方の開口部20にバイオセンサを挿入し、他方の開口部22に熱交換器21を挿入して、熱交換器21からバイオセンサを通過し外部に排出する試料液の配管系と、恒温槽ブロック19の底部に取り付けたシート状ヒーター4aと、恒温槽ブロック19を覆う断熱材およびこの断熱材を包み込む樹脂製ケースとを備えたものであり、恒温槽の熱媒体として水を用いる必要がなく、装置の保守管理が非常に容易になる。また、マグネティックスターラーを使用しないことから、占有体積が極めて小さく、コンパクトなものとする事ができる。



## 【特許請求の範囲】

【請求項1】生体機能物質を多孔性膜に固定した固定化膜を装着したフローセルと、電気化学的検出器（電極）とを組み合わせたバイオセンサにより、温度計と温度調節計を用いて所定温度に調節した試料液の成分分析を行なう装置のバイオセンサ用恒温槽であって、

a. 上面が開口した二つの開口部とこれらを連通させて側壁に抜ける配管溝を形成した金属製の恒温槽ブロック、

b. 前記恒温槽ブロックの一方の開口部に挿入したバイオセンサ、

c. 前記恒温槽ブロックの他方の開口部に挿入した熱交換器、

d. 試料液を導入し前記熱交換器から前記バイオセンサを通過して前記試料液を外部に排出する配管系、

e. 前記恒温槽ブロックの底部に取り付け前記恒温槽ブロックを所定の温度に設定する加熱手段、

f. 前記恒温槽ブロックを覆う断熱材およびこの断熱材を包み込む樹脂製ケースとを備えたことを特徴とするバイオセンサ用恒温槽。

【請求項2】請求項1記載のバイオセンサ用恒温槽において、バイオセンサは恒温槽ブロックの底面に垂直な方向に対して傾斜を有することを特徴とするバイオセンサ用恒温槽。

【請求項3】請求項1または2記載のバイオセンサ用恒温槽において、バイオセンサは恒温槽ブロックの一方の開口部内面に密着させて挿入することを特徴とするバイオセンサ用恒温槽。

【請求項4】請求項1ないし3記載のバイオセンサ用恒温槽において、熱交換器は一端が試料液を流入する配管に、他端がバイオセンサの配管に接続されるコイル状に形成したステンレスパイプを円柱状本体にに嵌め込んでなることを特徴とするバイオセンサ用恒温槽。

【請求項5】請求項1ないし4記載のバイオセンサ用恒温槽において、加熱手段としてシート状ヒーターを用いることを特徴とするバイオセンサ用恒温槽。

【請求項6】請求項1ないし4記載のバイオセンサ用恒温槽において、加熱手段としてペルチェ素子を用いることを特徴とするバイオセンサ用恒温槽。

## 【発明の詳細な説明】

## 【0001】

【産業上の利用分野】本発明は、酵素、微生物などを分子識別素子（レセプタ）として多孔性膜に固定した固定化膜によって試料液の成分分析を行なう装置のバイオセンサ用恒温槽に関する。

## 【0002】

【従来の技術】この種のバイオセンサは、試料液中の測定対象物質を認識する分子識別素子（レセプタ）として、酵素、微生物などの生体機能性物質を応用して多孔

検出器とを組み合わせ、試料液の成分分析を行なうセンサである。

【0003】このセンサは、試料液を固定化膜に接触させ、これによって生ずる生化学的反応による変化を、電極の出力電流として検出し、この計測値を演算し制御部で信号処理して得られる値を測定することを原理とするものであり、測定対象を生体機能性物質によって定めることができるという測定の選択性に優れている特徴を持つことから、血液検査における血糖値測定などの医療分野、食品の品質管理におけるアルコールの濃度測定などの発酵、食品工業計測や、廃水処理における水質測定などの環境計測分野などで利用されている。

【0004】一般にバイオセンサに使用されている酵素、微生物の反応性、成育速度、活性は温度により変化し、低温のときは活性が低く、高温になるにつれて活性が高まり、至適温度において活性が最大になり、さらに高温になると熱変性などにより熱失活し、活性が低下することが知られており、反応性、反応の安定性の面から、至適温度付近で用いることが望ましいとされている。バイオセンサもこれらの物質を応用しているため、当然温度によってバイオセンサの出力特性が変動するので、一定の温度条件で測定を行なう必要があり、従来、これに適するように装置を構成し温度を一定として測定を行なっている。

【0005】例えば、図6、図7、図8は特開平2-77641号公報に記載されている装置構成図であり、図6は図7のD-D線断面図、図7は図6のC-C線断面図を示し、また図8はこの装置の要部構成部材を分離して示した斜視図である。

【0006】図6～図8を併用参照してこの装置を説明する。図6～図8において温度計1により、恒温水槽2内の水の温度を検知し、温度調節器3によりヒーター4のオン・オフを制御することにより、この水の温度を所望の一定温度に保つ。この際、恒温水槽2内の水は、攪拌子5をマグネティックスターラー6で外部から回転させることにより攪拌され、熱交換効率を高めるように、このマグネティックスターラー6の上に恒温水槽2が載せられている。恒温水槽2内の上部に格納槽7が取り付けられており、この格納槽7内に固定化膜8を装着したフローセル9と、電気化学的検出器（電極）10とを組み合わせたバイオセンサ11を設けてあり、バイオセンサ11の信号線12が引き出されている。試料液13は、図示していない送液ポンプによって配管14aの流入口15から装置内に送液され、恒温水槽2内部に設けられた熱交換器16を通過して加温されてから、配管14bを経て格納槽7内の配管17aとフローセル9の配管17bとを通過して、バイオセンサ11により成分分析された後、流出口18から系外へ排出される。

## 【0007】

図8に示した従来の分析装置では、とくに恒温水槽2に関して次のような問題がある。即ち、恒温水槽2は熱媒として水を使用しているために、温度を一定にするには常に水の攪拌が必要であり、したがって、この水を攪拌するための攪拌子5とマグネティックスターラー6を用いなければならず、そのため、水の補給の必要性、攪拌子5の磨耗による恒温水槽2内部の汚れのために攪拌子5の定期的交換が必要となるなど、この装置の保守管理上の問題、さらに恒温水槽2とマグネティックスターラー6の両者が位置する占有体積が大きくなり、長期間使用時の維持管理が難しくなるという問題などが生ずることである。

【0008】本発明は上述の問題を解決するためになされたものであり、その目的はコンパクトで維持管理が容易であり、高い測定精度の得られるバイオセンサ用恒温槽を提供することにある。

【0009】

【課題を解決するための手段】上記の課題を解決するために、本発明のバイオセンサ用恒温槽は、上面が開口した二つの開口部とこれらを連通させて側壁に抜ける配管溝を形成した金属製の恒温槽ブロックと、この恒温槽ブロックの一方の開口部に挿入したバイオセンサと、恒温槽ブロックの他方の開口部に挿入した熱交換器と、試料液を導入し熱交換器からバイオセンサを通過して試料液を外部に排出する配管系と、恒温槽ブロックの底部に取り付け恒温槽ブロックを所定の温度に設定するヒーターと、恒温槽ブロックを覆う断熱材およびこの断熱材を包み込む樹脂製ケースとを備えたものである。

【0010】

【作用】本発明のバイオセンサ用恒温槽は上記のように構成し、金属製の恒温槽ブロックを用いて、バイオセンサの温度条件を一定にする機能と、バイオセンサのフローセルに流入する試料液を一定温度に保持する熱交換機能とを持つ恒温槽としたため、試料液を直接所定の温度に調節することが可能となり、恒温槽の熱媒体として水を用いる必要がなく、この水を攪拌するための攪拌子とマグネティックスターラーも不要であり、水の補給、攪拌子の定期的な交換などを行わずに済み、攪拌子の磨耗による内部の汚れもないので、装置の保守管理が非常に容易になる。また、本発明のバイオセンサ用恒温槽は、マグネティックスターラーを使用しないことから、占有体積が従来の恒温水槽に比べて極めて小さく、コンパクトなものとなることができる。

【0011】

【実施例】以下、本発明を実施例に基づき説明する。説明の便宜上以後に示す図は、図6～図8と共通する部材に同一符号を用いてある。図1は本発明の恒温槽の概念を説明するために、要部の構成部材を分離して示した斜視図である。図1において、恒温槽ブロック19は、上

1を挿入する開口部22を形成した金属製ブロックである。開口部20と開口部22の間を一部で連通させ、恒温槽ブロック19の端面に達する配管溝23は配管を通すためのものである。熱交換器21は例えば鍔付きのA1円柱の本体21aの外周に、熱交換のために十分な長さ形成したコイル状ステンレスパイプ24を嵌め込み、このステンレスパイプ24が本体21aから容易に抜けないように、これより径の大きい蓋21bを一端に固定したものであり、熱交換器21の上部に温度計1を内蔵している。恒温槽ブロック19の底面には、例えば発熱体をシリコンゴムに埋め込んだシート状のヒーター4aを取り付け、このヒーター4aと温度計1を図示してない温度調節器に接続し、所定の温度に制御することができる。

【0012】また、屋外で用いる場合には、ヒーター4aの代わりにペルチェ効果による加熱・冷却用の機能素子を取り付けることもできる。ペルチェ効果は異種の導体もしくは半導体の接点に電流を流したとき、ジュール熱以外に熱の発生または吸収の起こる現象であり、流す電流の向きを変えることにより、熱の発生と吸収は反対になる。したがって、本発明の恒温槽ではヒーター4aの代わりに、このペルチェ効果による機能素子と、電流の向きを反転することが可能な電源を備えた温度調節器を用いることにより、周囲温度が設定温度より高い場合には、ペルチェ効果による機能素子は冷却器として働き、周囲温度が設定温度より低くなれば電流の向きが反対となってヒーターとして働き、いずれの場合でも恒温槽の温度を精度よく一定に保持することができる。そのため、屋外のように温度が大きく変化し、季節によって設定温度に対して周囲温度の方が高くなる場所では、ペルチェ効果による機能素子をヒーター4aの代わりに用いることにより、安定で高精度な試料液の成分分析が可能となる。

【0013】図2は、本発明に用いられるバイオセンサ11の要部の構成を示す模式断面図である。図2において、フローセル9は、電気化学的検出器（電極）10、信号線12、酸素透過膜25、固定化膜8を、Oリング26a、26bによって固定し、バイオセンサ11を構成している。17aは試料液13をフローセル9に流入させる配管であり、17bは試料液13を系外に排出させる配管である。

【0014】図3、図4はいずれも本発明の恒温槽の模式断面図を示すものであり、以下、両図を参照して説明する。図3はバイオセンサ11を挿入した恒温槽ブロック19をバイオセンサ11の側からみた模式断面図であり、恒温槽ブロック19の周囲には、図1で図示を省略した断熱材27と、さらにこの断熱材27も含めて恒温槽ブロック19全体を格納する樹脂製ケース28により囲まれている状態を示している。ここでバイオセンサ1

試料液 13 がフローセル 9 を流れるとき、試料液 13 中には空気を含んでいるから、その気泡が試料液 13 の流れを邪魔するように働く。この点を考慮して、本発明では試料液 13 を滑らかに流すために、バイオセンサ 11 が恒温槽ブロック 19 の底面と垂直な方向に対して傾斜を持つように、あらかじめ恒温槽ブロック 19 の開口部を形成しておき、図 3 に示す如くバイオセンサ 11 を傾けて取り付けである。バイオセンサ 11 の傾斜角度は厳密に定める必要はないが、ほぼ 40° 程度が適当である。そしてバイオセンサ 11 は恒温槽ブロック 19 から

【0015】図 4 は図 3 の直角方向からみた本発明のバイオセンサ用恒温槽の模式断面図であり、試料液 13 は流入口 15 から導入され、熱交換器 21 内のステンレスパイプ 24 を通り、所定の温度に熱交換され、他方の配管 14 b から配管 17 a を通過して、バイオセンサ 11 に入り、図 2 に示したフローセル 9 の固定化膜 8 と接触した後、配管 17 b を経て流出口 18 から系外へ排出される。

【0016】図 5 はこのバイオセンサ用恒温槽の各部分の温度の測定結果を、縦軸を温度、横軸を経過時間として両者の関係を示した特性線図である。図 5 中、T<sub>1</sub> は熱交換器 21 入口における流入試料液 13 の温度、T<sub>2</sub> は同じく熱交換器 21 流出直後の試料液 13 の温度、T<sub>3</sub> はフローセル 9 の温度、T<sub>4</sub> は恒温槽ブロック 19 の周囲の気温を表わす。図 5 に示すように、流入する試料液 13 の温度 T<sub>1</sub> が 13℃ から 36℃ の範囲で変化したとき、熱交換器 21 流出直後の試料液 13 の温度 T<sub>2</sub> の値は、30.6℃ の +0.7℃、-0.5℃ 程度であり、バイオセンサ 11 の出力特性の変化を無視することができる範囲で、精度よく温度制御されている。また、前述のように流入する試料液 13 の温度が設定温度より高い場合には、ヒーター 4 a の代わりにペルチェ効果を持つ機能素子を用いて冷却することにより、高精度に温度制御することができることもわかった。

#### 【0017】

【発明の効果】バイオセンサ用の恒温槽は、従来、熱媒体として水を用いていたので、温度を一定にするために種々不都合な点を持っていたが、本発明では実施例で述べたように、金属製の恒温槽ブロックの二つの開口部に、それぞれバイオセンサと熱交換器とを挿入して、ブロック底部のシート状ヒーターを用いて昇温することにより、一定温度を得られる構造としたために、熱媒体として水を用いずに済ませることができるから、水を攪拌する攪拌子とマグネティックスターラーが不要となるばかりでなく、水の補給、攪拌子の磨耗による恒温槽の汚れ、攪拌子の定期的な交換など、メンテナンスに関す

た。さらにマグネティックスターラーを使用しないことから、占有体積が約 80% 程度も減少するので、非常に小さくコンパクトで保守管理が容易である。これらのことに加えて本発明によれば、試料液に対して高精度の温度制御が可能であり、精度の高い測定値を得ることができる。さらに、試料液の温度が設定温度より高いときには、ヒーターの代わりにペルチェ効果を持つ機能素子を用いて冷却することにより、同様の効果をもたらすことができる。

#### 【図面の簡単な説明】

【図 1】本発明の恒温槽の要部構成部材を分離して示した斜視図

【図 2】本発明に用いられるバイオセンサの要部構成を示す模式断面図

【図 3】本発明に用いられる恒温槽ブロックのバイオセンサ側からみた模式断面図

【図 4】本発明に用いられる恒温槽ブロックの図 3 と直角方向からみた模式断面図

【図 5】本発明の恒温槽に関する各部の温度特性線図

【図 6】従来の恒温水槽の模式断面図を示す図 7 の D-D 線断面図

【図 7】従来の恒温水槽の模式断面図を示す図 6 の C-C 線断面図

【図 8】従来の恒温水槽の要部構成部材を分離して示した斜視図

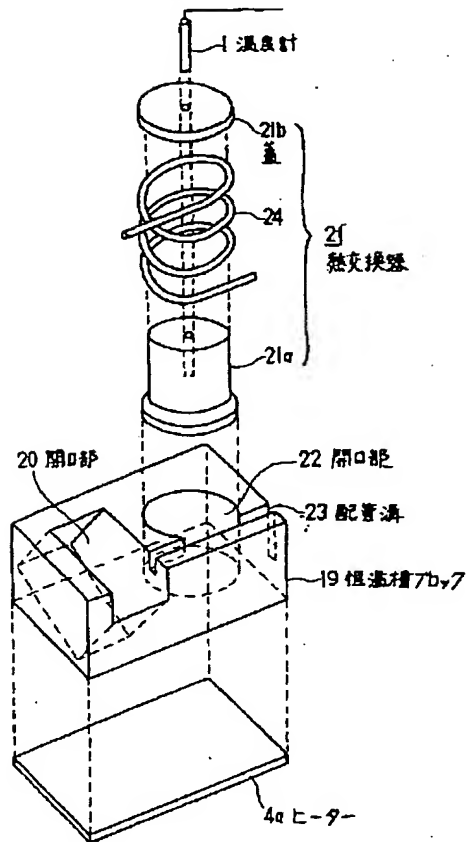
#### 【符号の説明】

- 1 温度計
- 2 恒温水槽
- 3 温度調節器
- 4 ヒータ
- 4 a ヒータ
- 5 攪拌子
- 6 マグネティックスターラー
- 7 格納槽
- 8 固定化膜
- 9 フローセル
- 10 電気化学的検出器（電極）
- 11 バイオセンサ
- 12 信号線
- 13 試料液
- 14 a 配管
- 14 b 配管
- 15 流入口
- 16 熱交換器
- 17 a 配管
- 17 b 配管
- 18 流出口
- 19 恒温槽ブロック
- 20 開口部

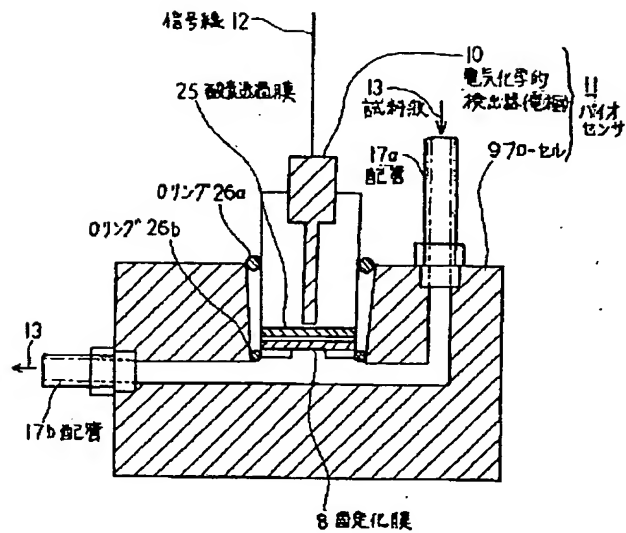
- 21 a 本体  
21 b 蓋  
22 開口部  
23 配管溝  
24 ステンレスパイプ

- 25 酸素透過膜  
26 a Oリング  
26 b Oリング  
27 断熱材  
28 ケース

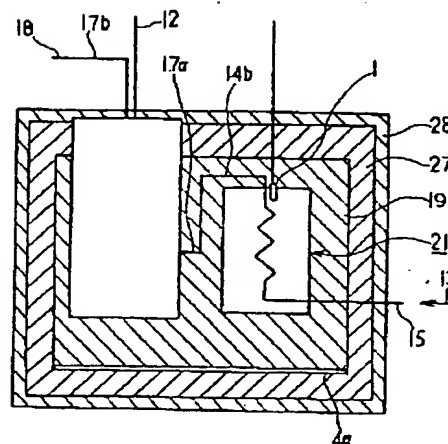
【図1】



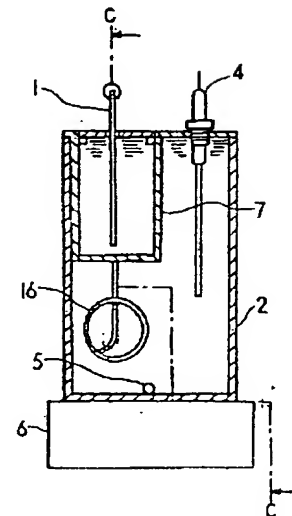
【図2】



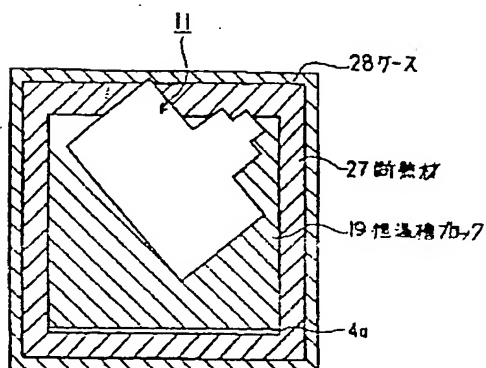
【図4】



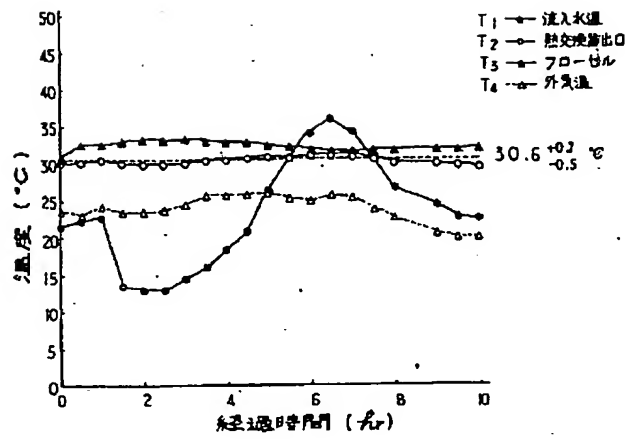
【図6】



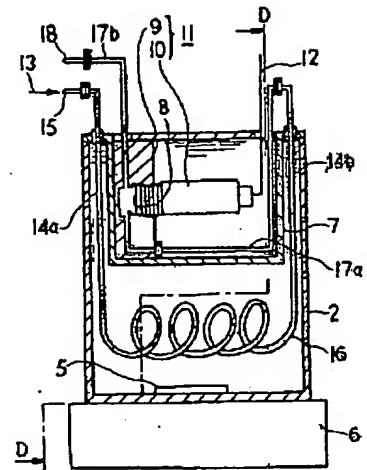
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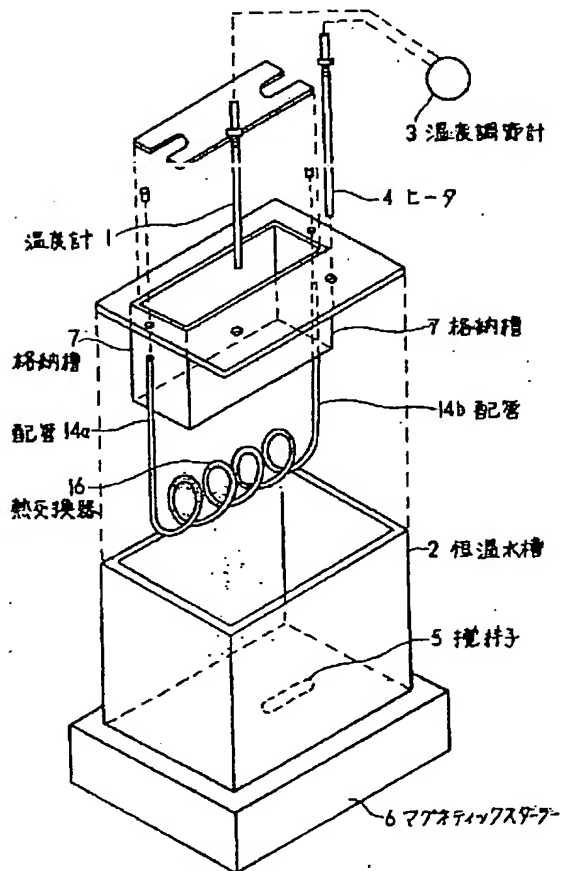
【図5】



【図7】



【図8】



# PATENT ABSTRACTS OF JAPAN

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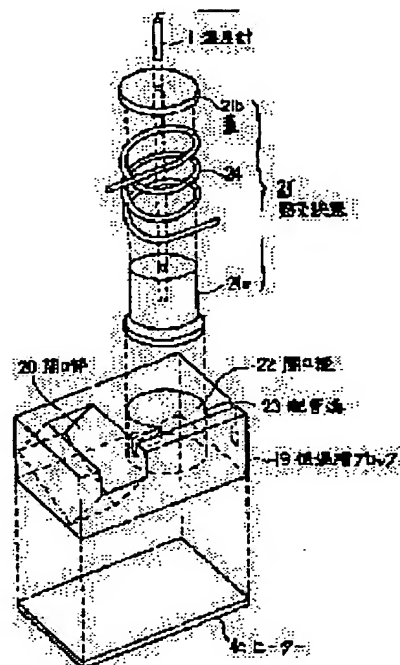
(72)Inventor : ISOBE KENSUKE  
TANAKA YOSHIHARU  
HOSHIKAWA HIROSHI

## (54) CONSTANT TEMPERATURE CHAMBER FOR BIOSENSOR

### (57)Abstract:

**PURPOSE:** To provide a compact constant temperature chamber whose maintenance is easy without using water as a heat medium, because a magnetic stirrer and an agitator are required, the occupying volume is large and much time is required in maintenance and control in a constant temperature chamber, wherein temperature is kept constant with water as a heat medium.

**CONSTITUTION:** In a constant temperature chamber for a biosensor, the parts for the following functions are provided. A biosensor is inserted into one opening part 20 of a metallic constant temperature chamber block 19. A heat exchanger 21 is inserted into another opening part 22. Sample liquid is made to pass through the biosensor from the heat exchanger 21 and discharged to the outside through a pipe. A heater 4a in a sheet shape is attached to the bottom part of the constant temperature chamber block 19. A heat insulating material covers the constant temperature chamber block 19. A case made of resin wraps the heat insulating material. It is not necessary to use water as a heat medium for the constant temperature chamber. The maintenance and control of the apparatus becomes very easy. Since a magnetic stirrer is not used, the occupying volume is very small, and the oven can be made compact.



## LEGAL STATUS

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CLAIMS

[Claim(s)]

[Claim 1] With the biosensor which combined the flow cell equipped with the fixed film which fixed the living body functional matter to the porous film, and the electrochemical detector (electrode) It is the thermostat for biosensors of the equipment which performs component analysis of the sample solution adjusted to predetermined temperature using the thermometer and the temperature controller. a. Metal thermostat block in which the piping slot from which a top face makes open for free passage two openings and these which carried out opening, and escapes on a side attachment wall was formed, b. The biosensor inserted in one opening of said thermostat block, the heat exchanger inserted in opening of another side of the c. aforementioned thermostat block, d. The pipe line which introduces a sample solution, passes said biosensor from said heat exchanger, and discharges said sample solution outside, e. A heating means to attach in the pars basilaris ossis occipitalis of said thermostat block, and to set said thermostat block as predetermined temperature, thermostat for biosensors characterized by having the case made of resin where a wrap heat insulator and this heat insulator are wrapped in for the f. aforementioned thermostat block.

[Claim 2] It is the thermostat for BAOSENSA characterized by a biosensor having an inclination to a direction perpendicular to the base of a thermostat block in the thermostat for biosensors according to claim 1.

[Claim 3] It is the thermostat for biosensors characterized by sticking a biosensor to one opening inside of a thermostat block in the thermostat for biosensors according to claim 1 or 2, and inserting.

[Claim 4] the thermostat for biosensors characterized by a heat exchanger looking like [ a cylindrical body ] the stainless steel pipe formed in the coiled form by which the other end is connected to piping of a biosensor, and coming to insert it in piping into which an end flows a sample solution in claim 1 thru/or the thermostat for biosensors given in three.

[Claim 5] The thermostat for biosensors characterized by using a sheet-like heater as a heating means in claim 1 thru/or the thermostat for biosensors given in four.

[Claim 6] The thermostat for biosensors characterized by using a Peltier device as a heating means in claim 1 thru/or the thermostat for biosensors given in four.

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## DETAILED DESCRIPTION

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### [Detailed Description of the Invention]

[0001]

[Industrial Application] This invention relates to the thermostat for biosensors of the equipment which performs component analysis of a sample solution with the fixed film fixed to the porous film by using an enzyme, a microorganism, etc. as a molecule discernment component (receptor).

[0002]

[Description of the Prior Art] This kind of biosensor is a sensor which performs component analysis of a sample solution combining the fixed film which applied living body functionality matter, such as an enzyme and a microorganism, and was fixed to the porous film as a molecule discernment component (receptor) which recognizes the measuring object matter in a sample solution, and the electrochemical detector which used the electrode.

[0003] This sensor change by the biochemical reaction which a sample solution is contacted on the fixed film and produced by this It is what makes it a principle to measure the value which detects as the output current of an electrode, calculates this measurement value, and is acquired by carrying out signal processing by the control section. From having the description excellent in the selectivity of measurement that the measuring object can be defined with the living body functionality matter It is used in the environmental measurement fields, such as fermentation, such as density measurement of the alcohol in quality control of the medical fields, such as blood sugar level measurement in a blood test, and food, food-stuff-industry measurement, and water quality measurement in waste water treatment, etc.

[0004] At the time of low temperature, activity increases as activity is low and becomes an elevated temperature, if activity becomes max and becomes an elevated temperature further in optimum temperature, thermal inactivation will be carried out by thermal denaturation etc., the reactivity of the enzyme currently generally used for the biosensor and a microorganism, a growth rate, and activity change with temperature, it is known that activity will fall, and it is made desirable from the field of reactivity and the stability of a reaction to use near optimum temperature. Since these matter is applied and the output characteristics of a biosensor are naturally changed with temperature, a biosensor also needs to measure on certain temperature conditions, and it is measuring by constituting equipment and setting temperature constant so that it may be suitable for this conventionally.

[0005] For example, drawing 6, drawing 7, and drawing 8 are equipment configuration Figs. indicated by JP,2-77641,A, drawing 6 shows D-D line sectional view of drawing 7, and drawing 7 shows the C-C line sectional view of drawing 6, and drawing 8 is the perspective view having separated and shown the important section configuration member of this equipment.

[0006] Concomitant use reference of drawing 6 - drawing 8 is carried out, and this equipment is explained. In drawing 6 - drawing 8, a thermometer 1 maintains the temperature of this water at a desired constant temperature by detecting the temperature of the water in a constant temperature bath 2, and controlling turning on and off of a heater 4 by the thermoregulator 3. Under the present circumstances, the water in a constant temperature bath 2 is stirred by rotating the stirring child 5 from the outside with a magnetic stirrer 6, and the constant temperature bath 2 is carried on this magnetic stirrer 6 so that heat exchange effectiveness may be raised. The storing tub 7 is attached in the upper part in a constant temperature bath 2, the biosensor 11 which combined the flow cell 9 equipped with the fixed film 8 and the electrochemical detector (electrode) 10 is formed in this storing tub 7, and the signal line 12 of a biosensor 11 is pulled out. The liquid is sent in equipment from the input 15 of piping 14a with the liquid-sending pump which is not illustrated, and after the sample solution 13 was warmed through the heat exchanger 16 prepared in the constant temperature bath 2 interior, it passes along piping 17a in the storing tub 7, and piping 17b of a flow cell 9 through piping 14b and component analysis is carried out with a biosensor 11, it is discharged out of a system from a tap hole 18.

[0007]

[Problem(s) to be Solved by the Invention] However, especially in the conventional analysis apparatus shown in drawing 6 – drawing 8 , there are the following problems about a constant temperature bath 2. Since the constant temperature bath 2 is using water as a heat carrier, stirring of water is always required to make temperature regularity, therefore the stirring child 5 and magnetic stirrer 6 for stirring this water must be used. Namely, that sake, Periodical exchange of the stirring child 5 is needed for the need for supply of water, and the dirt of the constant temperature bath 2 interior by the stirring child's 5 wear, It is that the problem that the problem on the maintenance control of this equipment and the occupied volume in which both constant temperature bath 2 and magnetic stirrer 6 are located further become large, and the maintenance at the time of prolonged use becomes difficult etc. arises.

[0008] It is made in order that this invention may solve an above-mentioned problem, and the purpose is compact, a maintenance is easy, and it is in offering the thermostat for biosensors with which the high accuracy of measurement is obtained.

[0009]

[Means for Solving the Problem] In order to solve the above-mentioned technical problem, the thermostat for biosensors of this invention Metal thermostat block in which the piping slot from which a top face makes open for free passage two openings and these which carried out opening, and escapes on a side attachment wall was formed, The biosensor inserted in one opening of this thermostat block, and the heat exchanger inserted in opening of another side of a thermostat block, The pipe line which introduces a sample solution, passes a biosensor from a heat exchanger, and discharges a sample solution outside, It has the heater which attaches in the pars basilaris ossis occipitalis of a thermostat block, and sets a thermostat block as predetermined temperature, and the case made of resin where a wrap heat insulator and this heat insulator are wrapped in for a thermostat block.

[0010]

[Function] The function which constitutes the thermostat for biosensors of this invention as mentioned above, and makes the temperature conditions of a biosensor regularity using a metal thermostat block, It writes as a thermostat with the heat exchange function to hold the sample solution which flows into the flow cell of a biosensor to constant temperature. It is not necessary to become possible to adjust a sample solution to direct predetermined temperature, and to use water as a heat carrier of a thermostat. Since the stirring child and magnetic stirrer for stirring this water are also unnecessary, it is not necessary to perform supply of water, periodical exchange of a stirring child, etc. and there is also no dirt of the interior by a stirring child's wear, the maintenance control of equipment becomes very easy. Moreover, since a magnetic stirrer is not used for the thermostat for biosensors of this invention, its occupied volume is very small compared with the conventional constant temperature bath, and can make it compact.

[0011]

[Example] Hereafter, this invention is explained based on an example. Drawing of explanation shown for convenience henceforth has used the same sign for the member which is common in drawing 6 – drawing 8 . Drawing 1 is the perspective view having separated and shown the configuration member of an important section, in order to explain the concept of the thermostat of this invention. In drawing 1 , the thermostat block 19 is a metal block in which the opening 20 which inserts a biosensor in a top face, and the opening 22 which inserts a heat exchanger 21 were formed. The piping slot 23 which is made to open between opening 20 and openings 22 for free passage partly, and reaches the end face of the thermostat block 19 is for letting piping pass. From this, a heat exchanger 21 fixes large lid 21b of a path to an end, and builds the thermometer 1 in the periphery of body 21a of aluminum cylinder with a collar in the upper part of a heat exchanger 21 so that the coiled form stainless steel pipe 24 formed in die length sufficient for heat exchange may be inserted in and this stainless steel pipe 24 may not fall out from body 21a easily. Heater 4a of the shape of a sheet which embedded the heating element at silicone rubber can be attached in the base of the thermostat block 19, and it can connect with the thermoregulator which is not illustrating this heater 4a and thermometer 1, and can control to predetermined temperature.

[0012] Moreover, when using outdoors, the functional device for heating / cooling by the Peltier effect can also be attached instead of heater 4a. A Peltier effect is the phenomenon in which generating of heat or absorption takes place in addition to the Joule's heat when a current is passed at the contact of a conductor of a different kind or a semi-conductor, and generating and absorption of heat become opposite by changing the sense of the current to pass. Therefore, by using the thermoregulator equipped with the functional device by this Peltier effect, and the power source which can reverse the sense of a current instead of heater 4a in the thermostat of this invention If the functional device according to a Peltier effect when an ambient temperature is higher than laying temperature works as a condensator and an ambient temperature becomes lower than laying temperature, the sense of a current can become opposite, and it can work as a heater, and, in any case, the temperature of a thermostat can be held often [ precision ] and uniformly. Therefore, temperature changes a lot like the outdoors and the component analysis of a stable

and highly precise sample solution becomes possible in the location where the direction of an ambient temperature becomes high to laying temperature according to a season by using the functional device by the Peltier effect instead of heater 4a.

[0013] Drawing 2 is the type section Fig. showing the configuration of the important section of the biosensor 11 used for this invention. In drawing 2, a flow cell 9 fixes an electrochemical detector (electrode) 10, a signal line 12, the oxygen transparency film 25, and the fixed film 8 with O rings 26a and 26b, and constitutes the biosensor 11. 17a is piping for which a sample solution 13 is made to flow into a flow cell 9, and 17b is piping which makes a sample solution 13 discharge out of a system.

[0014] Each of drawing 3 and drawing 4 shows the type section Fig. of the thermostat of this invention, and explains it with reference to both drawings hereafter. Drawing 3 is the type section Fig. which found the thermostat block 19 which inserted the biosensor 11 from the biosensor 11 side, and indicates the condition of being surrounded in the case 28 made of resin where the thermostat block 19 whole also including this heat insulator 27 is stored further to be the heat insulator 27 which omitted illustration by drawing 1 to the perimeter of the thermostat block 19. Since air is included in the sample solution 13 when a sample solution 13 will flow a flow cell 9, if a biosensor 11 is set to the base and perpendicular of the thermostat block 19 here, it works so that the air bubbles may interfere with the flow of a sample solution 13. In order to pass a sample solution 13 smoothly by this invention in consideration of this point, opening of the thermostat block 19 is formed beforehand, and as shown in drawing 3, a biosensor 11 is leaned and it has attached, so that a biosensor 11 may have an inclination to a direction perpendicular to the base of the thermostat block 19. Although it is not necessary to appoint whenever [ tilt-angle / of a biosensor 11 ] strictly, about about 40 degrees is suitable. And in order to improve heat conduction from the thermostat block 19, a biosensor 11 sticks a flow cell 9 and is inserted so that a touch area with the internal surface of the opening 20 of the thermostat block 19 may become as large as possible.

[0015] Drawing 4 is the type-section Fig. of the thermostat for biosensors of this invention seen from [ of drawing 3 ] the right angle, and a sample solution 13 is introduced from input 15, and passes along the stainless steel pipe 24 in a heat exchanger 21, and heat exchange is carried out to predetermined temperature, it passes piping 14b to piping 17a of another side, goes into a biosensor 11, and after it contacts the fixed film 8 of the flow cell 9 shown in drawing 2, it is discharged out of a system from a tap hole 18 through piping 17b.

[0016] Drawing 5 is the characteristic ray Fig. in which having made the axis of abscissa elapsed time for the measurement result of the temperature of each part of this thermostat for biosensors by having made the axis of ordinate into temperature, and having shown both relation. The inside of drawing 5, and T1 The temperature of the inflow sample solution 13 in heat exchanger 21 inlet port, and T2 Similarly they are the temperature of the sample solution 13 immediately after heat exchanger 21 outflow, and T3. The temperature of a flow cell 9, and T four The atmospheric temperature around the thermostat block 19 is expressed. Temperature T1 of the sample solution 13 which flows as shown in drawing 5 When it changes in 13 to 36 degrees C, it is the temperature T2 of the sample solution 13 immediately after heat exchanger 21 outflow. Values are 30.6 degrees C +0.7 degrees C and about -0.5 degrees C, and are the range which can disregard change of the output characteristics of a biosensor 11, and temperature control is improved them by precision. Moreover, when the temperature of the sample solution 13 which flows as mentioned above was higher than laying temperature, by cooling using the functional device which has a Peltier effect instead of heater 4a also showed that temperature control could be carried out with high precision.

[0017]

[Effect of the Invention] Although it had an inconvenient point variously in order to make temperature regularity since water was conventionally used for the thermostat for biosensors as a heat carrier By inserting a biosensor and a heat exchanger in two openings of a metal thermostat block, respectively, and carrying out a temperature up to them using the sheet-like heater of a block pars basilaris ossis occipitalis, as the example described in this invention Since water cannot be made to use as a heat carrier for writing as the structure where constant temperature can be obtained Periodical exchange of the dirt of the constant temperature bath by supply of water and a stirring child's wear and a stirring child etc. stopped the stirring child and magnetic stirrer which stir water not only becoming unnecessary, but needing a troublesome activity like before about a maintenance at all. Since a magnetic stirrer furthermore is not used and occupied volume decreases about 80%, it is very small compact and maintenance control is easy. In addition to these things, to a sample solution, highly precise temperature control is possible and, according to this invention, measured value with a high precision can be obtained. Furthermore, when the temperature of a sample solution is higher than laying temperature, the same effectiveness can be brought about by cooling using the functional device which has a Peltier effect instead of a heater.

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**TECHNICAL FIELD**

---

[Industrial Application] This invention relates to the thermostat for biosensors of the equipment which performs component analysis of a sample solution with the fixed film fixed to the porous film by using an enzyme, a microorganism, etc. as a molecule discernment component (receptor).

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PRIOR ART

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[Description of the Prior Art] This kind of biosensor is a sensor which performs component analysis of a sample solution combining the fixed film which applied living body functionality matter, such as an enzyme and a microorganism, and was fixed to the porous film as a molecule discernment component (receptor) which recognizes the measuring object matter in a sample solution, and the electrochemical detector which used the electrode.

[0003] This sensor change by the biochemical reaction which a sample solution is contacted on the fixed film and produced by this It is what makes it a principle to measure the value which detects as the output current of an electrode, calculates this measurement value, and is acquired by carrying out signal processing by the control section. From having the description excellent in the selectivity of measurement that the measuring object can be defined with the living body functionality matter It is used in the environmental measurement fields, such as fermentation, such as density measurement of the alcohol in quality control of the medical fields, such as blood sugar level measurement in a blood test, and food, food-stuff-industry measurement, and water quality measurement in waste water treatment, etc.

[0004] At the time of low temperature, activity increases as activity is low and becomes an elevated temperature, if activity becomes max and becomes an elevated temperature further in optimum temperature, thermal inactivation will be carried out by thermal denaturation etc., the reactivity of the enzyme currently generally used for the biosensor and a microorganism, a growth rate, and activity change with temperature, it is known that activity will fall, and it is made desirable from the field of reactivity and the stability of a reaction to use near optimum temperature. Since these matter is applied and the output characteristics of a biosensor are naturally changed with temperature, a biosensor also needs to measure on certain temperature conditions, and it is measuring by constituting equipment and setting temperature constant so that it may be suitable for this conventionally.

[0005] For example, drawing 6 , drawing 7 , and drawing 8 are equipment configuration Figs. indicated by JP,2-77641,A, drawing 6 shows D-D line sectional view of drawing 7 , and drawing 7 shows the C-C line sectional view of drawing 6 , and drawing 8 is the perspective view having separated and shown the important section configuration member of this equipment.

[0006] Concomitant use reference of drawing 6 - drawing 8 is carried out, and this equipment is explained. In drawing 6 - drawing 8 , a thermometer 1 maintains the temperature of this water at a desired constant temperature by detecting the temperature of the water in a constant temperature bath 2, and controlling turning on and off of a heater 4 by the thermoregulator 3. Under the present circumstances, the water in a constant temperature bath 2 is stirred by rotating the stirring child 5 from the outside with a magnetic stirrer 6, and the constant temperature bath 2 is carried on this magnetic stirrer 6 so that heat exchange effectiveness may be raised. The storing tub 7 is attached in the upper part in a constant temperature bath 2, the biosensor 11 which combined the flow cell 9 equipped with the fixed film 8 and the electrochemical detector (electrode) 10 is formed in this storing tub 7, and the signal line 12 of a biosensor 11 is pulled out. The liquid is sent in equipment from the input 15 of piping 14a with the liquid-sending pump which is not illustrated, and after the sample solution 13 was warmed through the heat exchanger 16 prepared in the constant temperature bath 2 interior, it passes along piping 17a in the storing tub 7, and piping 17b of a flow cell 9 through piping 14b and component analysis is carried out with a biosensor 11, it is discharged out of a system from a tap hole 18.

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## EFFECT OF THE INVENTION

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[Effect of the Invention] Although it had an inconvenient point variously in order to make temperature regularity since water was conventionally used for the thermostat for biosensors as a heat carrier By inserting a biosensor and a heat exchanger in two openings of a metal thermostat block, respectively, and carrying out a temperature up to them using the sheet-like heater of a block pars basilaris ossis occipitalis, as the example described in this invention Since water cannot be made to use as a heat carrier for writing as the structure where constant temperature can be obtained Periodical exchange of the dirt of the constant temperature bath by supply of water and a stirring child's wear and a stirring child etc. stopped the stirring child and magnetic stirrer which stir water not only becoming unnecessary, but needing a troublesome activity like before about a maintenance at all. Since a magnetic stirrer furthermore is not used and occupied volume decreases about 80%, it is very small compact and maintenance control is easy. In addition to these things, to a sample solution, highly precise temperature control is possible and, according to this invention, measured value with a high precision can be obtained. Furthermore, when the temperature of a sample solution is higher than laying temperature, the same effectiveness can be brought about by cooling using the functional device which has a Peltier effect instead of a heater.

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TECHNICAL PROBLEM

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[Problem(s) to be Solved by the Invention] However, especially in the conventional analysis apparatus shown in drawing 6 – drawing 8 , there are the following problems about a constant temperature bath 2. Since the constant temperature bath 2 is using water as a heat carrier, stirring of water is always required to make temperature regularity, therefore the stirring child 5 and magnetic stirrer 6 for stirring this water must be used. Namely, that sake, Periodical exchange of the stirring child 5 is needed for the need for supply of water, and the dirt of the constant temperature bath 2 interior by the stirring child's 5 wear, It is that the problem that the problem on the maintenance control of this equipment and the occupied volume in which both constant temperature bath 2 and magnetic stirrer 6 are located further become large, and the maintenance at the time of prolonged use becomes difficult etc. arises.

[0008] It is made in order that this invention may solve an above-mentioned problem, and the purpose is compact, a maintenance is easy, and it is in offering the thermostat for biosensors with which the high accuracy of measurement is obtained.

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**MEANS**

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[Means for Solving the Problem] In order to solve the above-mentioned technical problem, the thermostat for biosensors of this invention Metal thermostat block in which the piping slot from which a top face makes open for free passage two openings and these which carried out opening, and escapes on a side attachment wall was formed, The biosensor inserted in one opening of this thermostat block, and the heat exchanger inserted in opening of another side of a thermostat block, The pipe line which introduces a sample solution, passes a biosensor from a heat exchanger, and discharges a sample solution outside, It has the heater which attaches in the pars basilaris ossis occipitalis of a thermostat block, and sets a thermostat block as predetermined temperature, and the case made of resin where a wrap heat insulator and this heat insulator are wrapped in for a thermostat block.

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OPERATION

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[Function] The function which constitutes the thermostat for biosensors of this invention as mentioned above, and makes the temperature conditions of a biosensor regularity using a metal thermostat block, It writes as a thermostat with the heat exchange function to hold the sample solution which flows into the flow cell of a biosensor to constant temperature. It is not necessary to become possible to adjust a sample solution to direct predetermined temperature, and to use water as a heat carrier of a thermostat. Since the stirring child and magnetic stirrer for stirring this water are also unnecessary, it is not necessary to perform supply of water, periodical exchange of a stirring child, etc. and there is also no dirt of the interior by a stirring child's wear, the maintenance control of equipment becomes very easy. Moreover, since a magnetic stirrer is not used for the thermostat for biosensors of this invention, its occupied volume is very small compared with the conventional constant temperature bath, and can make it compact.

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EXAMPLE

[Example] Hereafter, this invention is explained based on an example. Drawing of explanation shown for convenience henceforth has used the same sign for the member which is common in drawing 6 – drawing 8. Drawing 1 is the perspective view having separated and shown the configuration member of an important section, in order to explain the concept of the thermostat of this invention. In drawing 1, the thermostat block 19 is a metal block in which the opening 20 which inserts a biosensor in a top face, and the opening 22 which inserts a heat exchanger 21 were formed. The piping slot 23 which is made to open between opening 20 and openings 22 for free passage partly, and reaches the end face of the thermostat block 19 is for letting piping pass. From this, a heat exchanger 21 fixes large lid 21b of a path to an end, and builds the thermometer 1 in the periphery of body 21a of aluminum cylinder with a collar in the upper part of a heat exchanger 21 so that the coiled form stainless steel pipe 24 formed in the length sufficient for heat exchange may be inserted in and this stainless steel pipe 24 may not fall out from body 21a easily. Heater 4a of the shape of a sheet which embedded the heating element at silicone rubber can be attached in the base of the thermostat block 19, and it can connect with the thermoregulator which is not illustrating this heater 4a and thermometer 1, and can control to predetermined temperature.

[0012] Moreover, when using outdoors, the functional device for heating / cooling by the Peltier effect can also be attached instead of heater 4a. A Peltier effect is the phenomenon in which generating of heat or absorption takes place in addition to the Joule's heat when a current is passed at the contact of a conductor of a different kind or a semi-conductor, and generating and absorption of heat become opposite by changing the sense of the current to pass. Therefore, by using the thermoregulator equipped with the functional device by this Peltier effect, and the power source which can reverse the sense of a current instead of heater 4a in the thermostat of this invention If the functional device according to a Peltier effect when an ambient temperature is higher than laying temperature works as a condensator and an ambient temperature becomes lower than laying temperature, the sense of a current can become opposite, and it can work as a heater, and, in any case, the temperature of a thermostat can be held often [ precision ] and uniformly. Therefore, temperature changes a lot like the outdoors and the component analysis of a stable and highly precise sample solution becomes possible in the location where the direction of an ambient temperature becomes high to laying temperature according to a season by using the functional device by the Peltier effect instead of heater 4a.

[0013] Drawing 2 is the type section Fig. showing the configuration of the important section of the biosensor 11 used for this invention. In drawing 2, a flow cell 9 fixes an electrochemical detector (electrode) 10, a signal line 12, the oxygen transparency film 25, and the fixed film 8 with O rings 26a and 26b, and constitutes the biosensor 11. 17a is piping for which a sample solution 13 is made to flow into a flow cell 9, and 17b is piping which makes a sample solution 13 discharge out of a system.

[0014] Each of drawing 3 and drawing 4 shows the type section Fig. of the thermostat of this invention, and explains it with reference to both drawings hereafter. Drawing 3 is the type section Fig. which found the thermostat block 19 which inserted the biosensor 11 from the biosensor 11 side, and indicates the condition of being surrounded in the case 28 made of resin where the thermostat block 19 whole also including this heat insulator 27 is stored further to be the heat insulator 27 which omitted illustration by drawing 1 to the perimeter of the thermostat block 19. Since air is included in the sample solution 13 when a sample solution 13 will flow a flow cell 9, if a biosensor 11 is set to the base and perpendicular of the thermostat block 19 here, it works so that the air bubbles may interfere with the flow of a sample solution 13. In order to pass a sample solution 13 smoothly by this invention in consideration of this point, opening of the thermostat block 19 is formed beforehand, and as shown in drawing 3, a biosensor 11 is leaned and it has attached, so that a biosensor 11 may have an inclination to a direction perpendicular to the base of the thermostat block 19. Although it is not necessary to appoint whenever [ tilt-angle / of a biosensor 11 ] strictly, about about 40 degrees is suitable. And in order to improve heat conduction from the thermostat block 19, a biosensor 11 sticks a flow cell 9 and is inserted so that a touch area with the internal surface

of the opening 20 of the thermostat block 19 may become as large as possible.

[0015] Drawing 4 is the type-section Fig. of the thermostat for biosensors of this invention seen from [ of drawing 3 ] the right angle, and a sample solution 13 is introduced from input 15, and passes along the stainless steel pipe 24 in a heat exchanger 21, and heat exchange is carried out to predetermined temperature, it passes piping 14b to piping 17a of another side, goes into a biosensor 11, and after it contacts the fixed film 8 of the flow cell 9 shown in drawing 2 , it is discharged out of a system from a tap hole 18 through piping 17b.

[0016] Drawing 5 is the characteristic ray Fig. in which having made the axis of abscissa elapsed time for the measurement result of the temperature of each part of this thermostat for biosensors by having made the axis of ordinate into temperature, and having shown both relation. The inside of drawing 5 , and T1 The temperature of the inflow sample solution 13 in heat exchanger 21 inlet port, and T2 Similarly they are the temperature of the sample solution 13 immediately after heat exchanger 21 outflow, and T3. The temperature of a flow cell 9, and T four The atmospheric temperature around the thermostat block 19 is expressed. Temperature T1 of the sample solution 13 which flows as shown in drawing 5 When it changes in 13 to 36 degrees C, it is the temperature T2 of the sample solution 13 immediately after heat exchanger 21 outflow. Values are 30.6 degrees C +0.7 degrees C and about -0.5 degrees C, and are the range which can disregard change of the output characteristics of a biosensor 11, and temperature control is improved them by precision. Moreover, when the temperature of the sample solution 13 which flows as mentioned above was higher than laying temperature, by cooling using the functional device which has a Peltier effect instead of heater 4a also showed that temperature control could be carried out with high precision.

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[Translation done.]

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1. This document has been translated by computer. So the translation may not reflect the original precisely.

2. \*\*\*\* shows the word which can not be translated.

3. In the drawings, any words are not translated.

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**DESCRIPTION OF DRAWINGS**

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[Brief Description of the Drawings]

[Drawing 1] The perspective view having separated and shown the important section configuration member of the thermostat of this invention

[Drawing 2] The type section Fig. showing the important section configuration of the biosensor used for this invention

[Drawing 3] The type section Fig. seen from the biosensor side of the thermostat block used for this invention

[Drawing 4] The type section Fig. seen from drawing 3 and the direction of a right angle of the thermostat block used for this invention

[Drawing 5] The temperature characteristic diagram of each part about the thermostat of this invention

[Drawing 6] D-D line sectional view of drawing 7 showing the type section Fig. of the conventional constant temperature bath

[Drawing 7] The C-C line sectional view of drawing 6 showing the type section Fig. of the conventional constant temperature bath

[Drawing 8] The perspective view having separated and shown the important section configuration member of the conventional constant temperature bath

[Description of Notations]

1 Thermometer

2 Constant Temperature Bath

3 Thermoregulator

4 Heater

4a Heater

5 Stirring Child

6 Magnetic Stirrer

7 Storing Tub

8 Fixed Film

9 Flow Cell

10 Electrochemical Detector (Electrode)

11 Biosensor

12 Signal Line

13 Sample Solution

14a Piping

14b Piping

15 Input

16 Heat Exchanger

17a Piping

17b Piping

18 Tap Hole

19 Thermostat Block

20 Opening

21 Heat Exchanger

21a Body

21b Lid

22 Opening

23 Piping Slot

24 Stainless Steel Pipe

25 Oxygen Transparency Film

26a O ring  
26b O ring  
27 Heat Insulator  
28 Case

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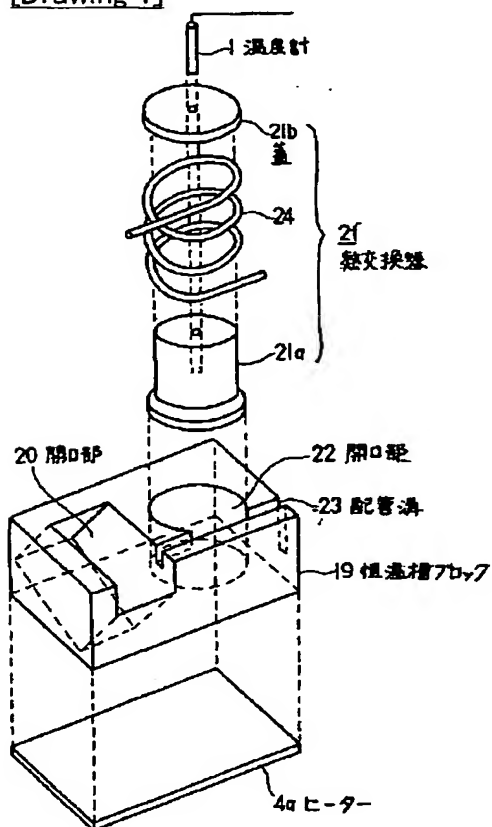
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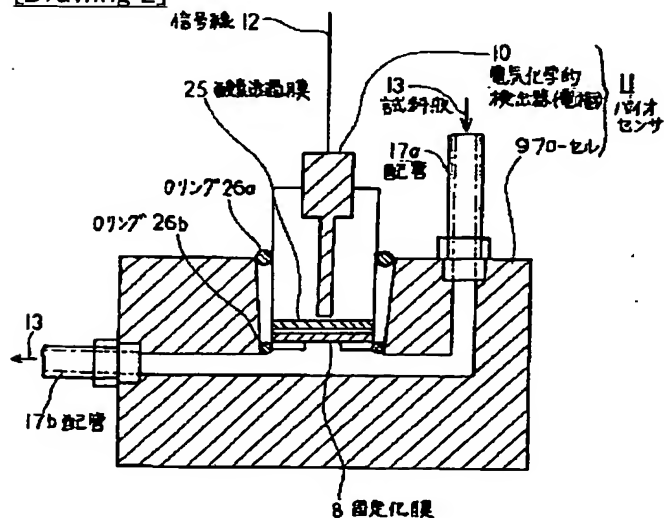
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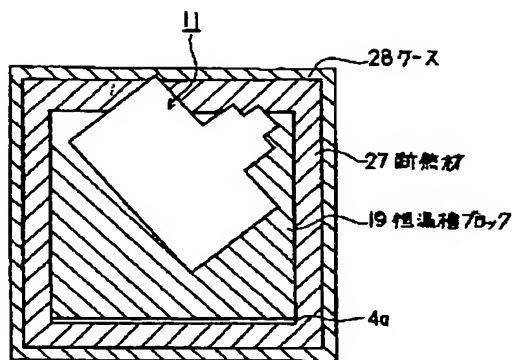
**[Drawing 1]**



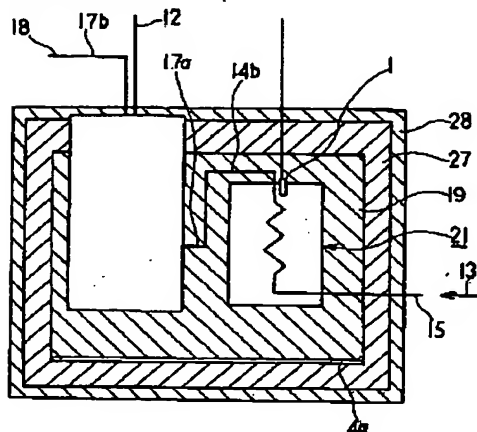
[Drawing 2]



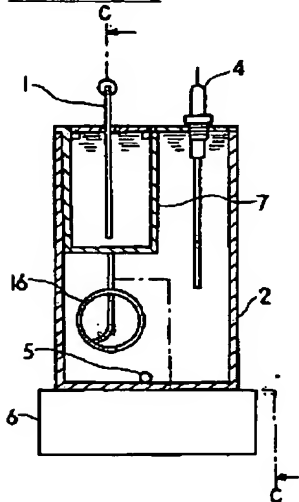
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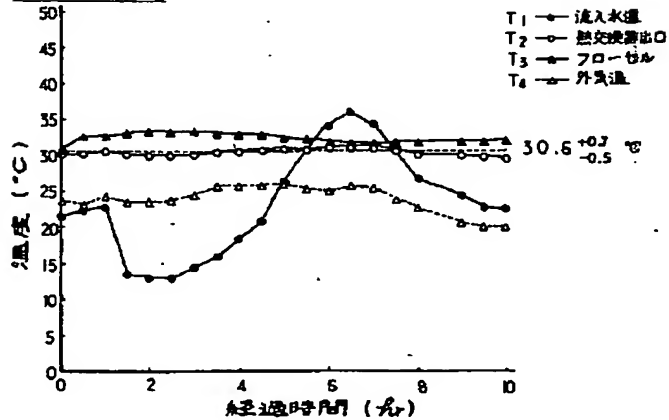
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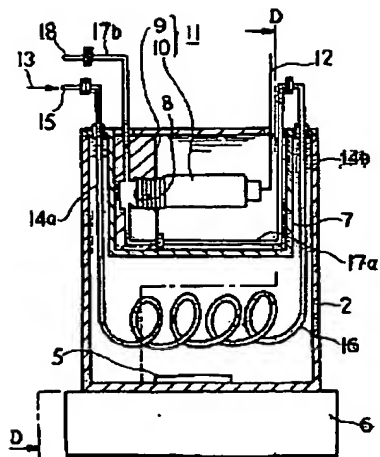
[Drawing 6]



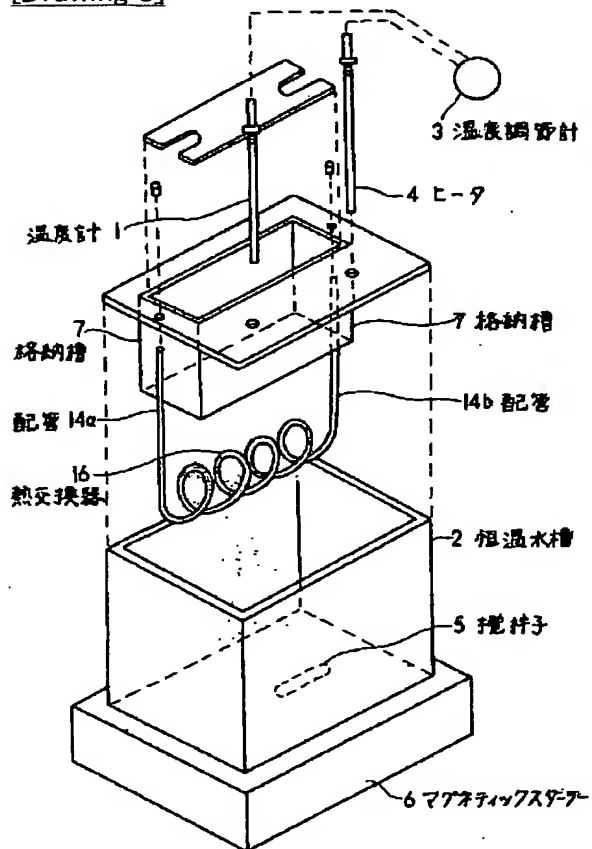
[Drawing 5]



[Drawing 7]



[Drawing 8]



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